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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
BRUMBACK, BRENDA G	
ART UNIT	PAPER NUMBER
1642	9

DATE MAILED: 06/06/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/677,653	CHRISTIAN ET AL.	
	Examiner	Art Unit	
	Brenda G. Brumback	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 March 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-24* is/are pending in the application.

4a) Of the above claim(s) *24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. *08/089,372* .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I, claims 15-23, in Paper No. 8, is acknowledged. The traversal is on the ground(s) that concurrent examination of the claims of Groups I and II would not place an undue burden upon the examiner. This is not found persuasive because the claim of Group II has a different classification than the claims of Group I. The search for Group II is not required for Group I. Examination of both groups together would entail separate and distinct searches and would thus constitute an undue burden upon the examiner. The requirement is still deemed proper and is therefore made FINAL.

Claims 15-24 are pending. Claim 24 is withdrawn from consideration as directed to a non-elected invention. Claims 15-23 are under examination on the merits.

Sequence Disclosures

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

APPLICANT IS GIVEN THE SAME TIME PERIOD AS THAT GIVEN TO REPLY TO THE PRESENT OFFICE ACTION WITHIN WHICH TO COMPLY WITH THE SEQUENCE RULES, 37 CFR 1.821 - 1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136. In no case may an applicant extend the period for response beyond the six month statutory

period. Applicant is requested to return a copy of the attached Notice to Comply with the response.

Since the instant application is a divisional of 08/485,355, this requirement may be fulfilled by submission of a letter requesting use of the previously filed sequence information in the instant application. The letter must completely identify the parent application by application number and the CRF, by indicating whether it was the only CRF filed in that application or whether it was the second or subsequent CRF filed. See MPEP 2422.05.

Information Disclosure Statement

The Information Disclosure Statement filed 01/22/2001 has been considered. A signed copy of the PTO 1449 form is attached hereto.

Specification

The disclosure is objected to because of the following informality: the continuing data listed in the first paragraph is incomplete, as it does not reference all of the parent applications.

Appropriate correction is required.

Claim Objections

Claims 15-23 are objected to because they lack proper introduction. The present Office practice is to insist that each claim be the object of a sentence starting with a phrase such as "I (or we) claim" or "What is claimed is" or "That which is claimed is". See MPEP 608.01 (m). Appropriate correction is required.

Claim 18 is objected to for an informality in the written format for the sequence identifier. The sequence identifier should be written SEQ ID NO:50.

Claim Rejections - 35 USC § 112

Claims 15-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The instant claims recite an isolated nucleic acid molecule comprising a first sequence encoding at least one capsid protein of an insect small RNA virus and a second sequence which is insecticidal or which encodes an insecticidal protein toxin. The claims are indefinite because the metes and bounds of "a second sequence which is insecticidal" are not clear. While the specification discloses protein toxins which are insecticidal, it fails to delineate other insecticidal sequences. Absent such disclosure, the metes and bounds of the claims cannot be determined and the claims are indefinite.

Claim 17 recites "HaSV" without identification of the full name of the virus which is denoted by the abbreviation. For clarification, it is suggested that at the first occurrence in the claims, the virus name be written as *Helicothis armigera* (or *Helioverpa armigera*) stunt virus. Further, it is unclear if the correct name for the virus is *Helicothis armigera* or *Helioverpa armigera*, as the specification appears to disclose both interchangeably (see page 3, lines 22-23, and page 11, first paragraph, for example).

Claim 18 is indefinite for recitation of "P71" by molecular weight without denoting the source of the protein, as many proteins from various sources may have the same molecular weight and hence, the same designation as "P71". It is suggested that the claim be amended to recite HaSV P71 or other appropriate term designating the protein source.

Claim 21 is vague and indefinite for recitation of "an antisense sequence" and a "mimicking structure", as the specification fails to disclose the metes and bounds of such sequences and structures.

Claims 15, 21, and 22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a "written description" rejection, rather than an enablement rejection under 35 U.S.C. 112, first paragraph. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Vas-Cath Inc. V. Mahurka, 19 USPQ2d 1111, states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention, for purposes of the "written description" inquiry, is *whatever is now claimed*" (see page 1117).

A review of the language of the claim indicates that these claims are drawn to a genus of nucleic acid molecules incorporating insecticidal sequences, antisense sequences, and mimicking structures. A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In *Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the

genus. The court indicated that, while applicants are not required to disclose every species encompassed by a genus, the description of the genus is achieved by the recitation of a representative number of species falling within the scope of the claimed genus. At section B(1), the court states "An adequate written description of a DNA ... requires a precise definition, such as by structure, formula, chemical name, or physical properties, not a mere wish or plan for obtaining the claimed chemical invention".

There is a single species of the claimed genus disclosed that is within the scope of the claimed genus, *i.e.,* nucleic acid molecules incorporating an insecticidal protein toxin. The disclosure of a single disclosed species may provide an adequate written description of a genus when the species disclosed is representative of the genus. However, the present claims encompass numerous species that are not further described. There is substantial variability among the species. One of skill in the art would not recognize from the disclosure that the applicant was in possession of the genus of which comprises nucleic acid molecules incorporating any and all insecticidal sequences, antisense sequences, and mimicking structures. The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (see *Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1115).

Claims 15-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for isolated nucleic acid sequences comprising a first sequence encoding a capsid protein of an insect RNA virus and a second sequence encoding an insecticidal protein toxin or a ribozyme, does not reasonably provide enablement for nucleic acid sequences comprising a second sequence encoding other insecticidal molecules, antisense sequences, or mimicking structures. The specification does not enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The first paragraph of 35 U.S.C. 112 states, "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same...". The courts have interpreted this to mean that the specification must enable one skilled in the art to make and use the invention without undue experimentation. The courts have further interpreted undue experimentation as requiring "ingenuity beyond that to be expected of one of ordinary skill in the art" (Fields v. Conover, 170 USPQ 276 (CCPA 1971)) or requiring an extended period of experimentation in the absence of sufficient direction or guidance (In re Colianni, 195 USPQ 150 (CCPA 1977)). Additionally, the courts have determined that "... where a statement is, on its face, contrary to generally accepted scientific principles", a rejection for failure to teach how to make and/or use is proper (In re Marzocchi, 169 USPQ 367 (CCPA 1971). Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Colianni, 195 USPQ 150, 153 (CCPA 1977) and have been clarified by the Board of Patent Appeals and Interferences in Ex parte Forman, 230 USPQ 546 (BPAI 1986). Among the factors are the nature of the invention, the state of the prior art, the predictability or lack thereof in the art, the amount of direction or guidance present, the presence or absence of working examples, the breadth of the claims, and the quantity of experimentation needed. The instant disclosure fails to meet the enablement requirement for the following reasons:

The nature of the invention: The claimed invention is drawn to isolated nucleic acid sequences comprising a first sequence encoding a capsid protein of an insect RNA virus and a second sequence encoding an insecticidal protein toxin, an insecticidal, a ribozyme, an antisense sequence, or a mimicking structure.

The state of the prior art and the predictability or lack thereof in the art: The art teaches insecticides comprising fusion proteins incorporating insect gut cell recognition or binding proteins with ribozymes or protein toxins and further teaches nucleic acid molecules encoding the fusion proteins (see Wilcox et al., U.S. Patent 6,051,556, especially the abstract; column 1, lines 10-20 and 44-49; and column 3, lines 24-32). The art also teaches that the capsids of insect viruses possess insect gut recognition or binding sequences (see Christian et al., IDS reference, especially page 144, first full paragraph, through page 146, first partial paragraph). The art does not teach, however, fusion proteins comprising insecticides other than toxins, antisense sequences, or mimicking structures.

The amount of direction or guidance present and the presence or absence of working examples: Given the teachings of unpredictability which are found it the art regarding fusion proteins incorporating insecticides other than toxins or ribozymes, antisense sequences, and mimicking structures, detailed teachings are needed in the specification to overcome those teachings of unpredictability. Such teachings are absent. The specification discloses and the working examples are specifically directed to fusion proteins incorporating proteins of an insect small RNA virus (HaSV) and a protein toxin or ribozyme. There is no guidance provided as to how to make nucleic acid molecules encoding fusion proteins incorporating an insect gut recognition sequence with any antisense molecules, any mimicking structures, or any insecticides other than protein toxins or ribozymes.

The breadth of the claims and the quantity of experimentation needed: Given the teachings of unpredictability which are found in the art and in the absence of sufficient disclosure in the specification to overcome those teachings of unpredictability, one of skill in the art would be unable to make or use the claimed invention commensurate in scope with the claims absent undue experimentation.

Priority

It is noted that the present application is a divisional of 08/485,355, filed 06/07/1995, now U.S. Patent 6,177,075; which is a continuation of 08/440,522, filed 05/12/1995; which is turn is a continuation-in-part of 08/089,372 filed 07/08/1993; which claims priority to Australian application PL4081/92 filed 08/14/1992. A review of the parent application shows support for the presently claimed subject matter in parent applications 08/485,355 filed 06/07/1995 and 08/440,552 filed 05/12/1995; however, while support for HaSV particles incorporating heterologous nucleic acids from toxins or other viruses and for fusion proteins incorporating capsid binding domains with other proteins was found, no support was found for the presently claimed isolated nucleic acid molecules encoding fusion proteins incorporating a capsid protein (P71) of an insect small RNA virus (HaSV) with an insecticidal protein toxin (Ricin A) *per se*. For this reason, the priority date for the present claims has been determined to be that of application 08/440,522 filed 05/12/1995. Applicant is invited to specifically point out where in the earlier filed applications support for the subject matter as is presently claimed can be found.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 15-23 are rejected under 35 U.S.C. 102(b) as being anticipated by Christian et al. (WO 94/04660).

The claimed invention is drawn to an isolated nucleic acid molecule comprising a first sequence encoding at least one capsid protein (P71, SEQ ID NO:50) of an insect small RNA virus

(HaSV) and a second sequence which encodes a ribozyme or an insecticidal protein toxin (Ricin A).

Christian et al. teach isolated nucleic acid molecules encoding fusion proteins incorporating an HaSV capsid protein (the P71 protein, for a preferred embodiment) and a ribozyme or toxin (ricin, for one embodiment) (see the abstract, page 12, lines 21-24; page 18, lines 4-12; page 70, lines 10-19, and page 72, lines 1-9).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 15-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wilcox et al. in view of Hanzlik et al. (Journal of General Virology 74:1805-1810, 1993, IDS reference).

The claimed invention is as described *supra*.

Wilcox et al. teach isolated nucleic acid molecules encoding hybrid pesticidal toxins (see the abstract). Wilcox et al. teach the hybrid toxins as encompassing a cytotoxic agent and a specific insect gut cell recognition or binding protein to direct the cytotoxic agent to the host target (see column 1, lines 17-20 and 44-49). Wilcox et al. teach the cytotoxic agent as a ribozyme (ribosome inactivator), with ricin listed as a specific embodiment (see column 3, lines 24-32). Wilcox et al. do not teach the insect gut cell recognition sequence as a small RNA virus capsid protein.

Hanzlik et al. teach a small RNA virus (HaSV) that is pathogenic to *Helicoverpa armigera*, infecting the insect via the gut. Hanzlik et al. teach *Helicoverpa armigera* are

economically important agricultural pests and that the viruses are potentially useful as biological control agents (see page 1805, the abstract and first two paragraphs, and pages 1809-1810, last paragraph). Hanzlik et al. teach an HaSV 70K protein (see page 1807, first full paragraph, and the paragraph bridging pages 1807 and 1808). Although Hanzlik et al. do not teach the amino acid sequence of the 70K protein, absent some evidence to the contrary, the protein would inherently have comprised the amino acid sequence set forth as SEQ ID NO:50.

One of ordinary skill in the art at the time the invention was made would have found it *prima facie* obvious to have incorporated an HaSV protein into an immunotoxin in order to make a hybrid pesticidal toxin, according to the teachings of Wilcox et al. One of ordinary skill in the art at the time the invention was made would have been motivated to do so in order to develop a hybrid immunotoxin for control of the agriculturally important pest, *H. armigera.*

Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Wilcox et al. in view of Hanzlik et al., as applied to claims 15-23 above and further in view of Hanzlik et al. (Journal of General Virology 74/4:799-811, April 1995; hereinafter Hanzlik 1995).

The claimed invention has been described *supra.*

As was set forth *supra*, Wilcox et al. teach hybrid immunotoxins comprising an insect gut recognition or binding sequence with an insecticidal toxin or ribozyme. Hanzlik et al. teach that the HaSV is an insect small RNA virus which infects *H. armigera* via the gut. Hanzlik et al. teach that the virus comprises a 70K protein, but do not teach the amino acid sequence of the protein.

Hanzlik 1995 teaches the complete nucleotide sequence of HaSV and specifically teaches the amino acid sequence of the 71kDa coat protein.

One of ordinary skill in the art at the time the invention was made would have found it *prima facie* obvious to have incorporated a nucleic acid encoding the P71 protein, according to

the teachings of Hanzlik et al., into the hybrid immunotoxin taught by Wilcox et al., in order to develop a hybrid immunotoxin effective against *H. armigera*.

Claims 15, 16, and 19-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wilcox et al. in view of Harley et al. (Virology 69:323-326, 1976, of record as IDS reference).

The claimed invention is drawn to an isolated nucleic acid molecule comprising a first sequence encoding at least one capsid protein of an insect small RNA virus (HaSV) and a second sequence encoding a ribozyme or an insecticidal protein toxin (Ricin A).

Wilcox et al. teach a hybrid immunotoxin comprising an insect gut recognition or binding protein and an insecticidal toxin. Wilcox et al. do not teach the insect gut recognition as derived from a capsid protein of an insect small RNA virus.

Harley et al. teach a cytoplasmic RNA virus which infects *H. armigera* (see page 323, the abstract and first paragraph), wherein it infects the gut (see page 323, second paragraph).

One of ordinary skill in the art at the time the invention was made would have found it *prima facie* obvious to have incorporated one or more capsid proteins from the RNA virus described by Harley et al. into the hybrid immunotoxin taught by Wilcox et al. in order to make an effective biological control agent for the agriculturally important pest, *H. armigera.*

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brenda Brumback whose telephone number is (703) 306-3220. If the examiner can not be reached, inquiries can be directed to Supervisory Patent Examiner Anthony Caputa whose telephone number is (703) 308-3995. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Examiner Brenda Brumback, Art Unit 1642 and should be marked "OFFICIAL" for entry into prosecution history or "DRAFT"

for consideration by the examiner without entry. The Official FAX telephone number is (703) 872-9306 and the After Final FAX telephone number is (703) 872-9307. FAX machines will be available to receive transmissions 24 hours a day. In compliance with 1096 OG 30, the filing date accorded to each OFFICIAL fax transmission will be determined by the FAX machine's stamped date found on the last page of the transmission, unless that date is a Saturday, Sunday or Federal Holiday with the District of Columbia, in which case the OFFICIAL date of receipt will be the next business day.

Brenda Brumback
Patent Examiner